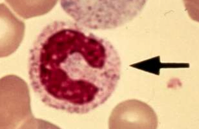
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| **LEUKEMIAS** | | | | | | | | | | | | | | | |
| **Acute Leukemias** | | | | | | | | | | | | | | | |
| Name | | Mutation | | | Diagnosis | | Signs/Symptoms | | | | Treatment/Prognosis | | | Other Notes | |
| **Acute Leukemias in General** | | —clonal ↑ in BLASTS in BM and peripheral blood  --rapid onset (day—weeks)  need immediate tx or death   * Neutropenia—bacterial infections, fever * Anemia: fatigue no energy * Thrombocytopenia: bleeding, petechiae, epistaxis, gum bleeding * Maybe hepatosplenomegaly, lymphadenopathy (in ALL), bone pain, possibly asx   Work-up   * GET A CBC and BM exam!!!! * Peripheral blood smear w/ differential count (blast %?) * BM exam—what is blast %? | | | | | | | | * + Special stains     - AML-myeloperoxidase +     - ALL—Tdt +   + Flow cytometry tells what surface Ag pattern     - T cells—CD1🡪8     - B cells CD 19🡪23     - Monocytic CD14     - Myeloid—CD11c, 13, 33     - Stem cells/blast—CD 34 * Genetics | | | | | |
| **Acute Lymphoblastic Leukemia (ALL)**   * Children <15 yrs | | * **t(8;14)**, t(2;**8**), t(8;22), always **8** 🡪 c-myc oncogene * t(9:22) has worse prognosis than in CML bad prognosis b/c makes p190 TK   + if you see a 210 TK then you know it was CML that progressed to ALL | | | | * **More than 20% or more blasts in marrow or peripheral blood** | | * Lymphadenopathy * CNS involvement (meningeal signs, headache, vomiting) more common in ALL than AML | | * Most common genetic abnormatlities are hyperdiploidy * t(12;21)—good prog   + t (9;22) –bad prognosis | | | * Classification * **L1**: Small blasts (Tdt+) * **L2**: Large blasts (Tdt+) * **L3**: Peripheral B, Burkitt leukemia/lymphoma   + **Tdt negative**   + Multiple vacuoles   + **t(8;14)**, t(2;**8**), t(8;22), always **8** 🡪 c-myc oncogene | | |
| **Acute Myelogenous Leukemia (AML)**   * 15-40 year olds | | * **M3: acute promyolocytic leukemia APL, multiple Auer rods ↑** (auer rods are seen in myeloblasts not lymphoblasts)   + **t(15;17)** 🡪 **PML blocks differentiation**   + **Treat with ATRA to promote differentiation**   + **Severe DIC due to dying PMN granules** * all AML regardless of blast count   + t(8;21)   + t(15;17)     - t(15;17) involves PML fusion w/ RARα and blocks differentiation   + inv 16 or t(16;16) * mutation in 11q23 gene is major regulator of hematopoiesis 🡪 poor prognosis | | | | * **More than 20% blasts in marrow** * AUER RODS   + Singe = AML not ALL   + multiple auer rods then APL   + Macintosh HD:Users:elisafuray:Desktop:Screen Shot 2012-12-20 at 9.09.24 AM.png | | * Neutropenia: bact infections, fever * Anemia * Thrombocytopenia: bleeding, petechiae, epistaxis * Maybe hepatosplenomegaly, lymphadenopathy(in ALL) * Bone pain * Can be asymptomatic | | * **APL**🡪**t(15;17) Treat with ATRA to promote differentiation** * t(8:21) and inv (16) or t(16;16) favorable prognosis | | | * Classification * **M0**: stem cells * **M1**: w/o maturation, >90% blasts * **M2**: with maturation, 20-90% blasts   + t(8;21) or t(16;16) 🡪 CFB blocks differentiation * **M3: acute promyolocytic leukemia APL, multiple Auer rods ↑** (auer rods are seen in myeloblasts not lymphoblasts)   + **t(15;17)** 🡪 **PML blocks differentiation**   + **Treat with ATRA to promote differentiation**   + **Severe DIC due to dying PMN granules** * **M4:** myelomonocytic, Inv16 subset associated w/ eosinophilia (M4eo) * **M5:** monocytic   + Gingival hyperplasia (many bacteria in mouth) * **M6:** Erythroleukemia * **M7:** Megakaryocytic   + Myelofibrosis common   + Increased in kids w/down syndrome | | |
| **Myelodysplastic Syndrome (MDS)**   * 40—60 y/o | | * Common genetic abnormalities   + -5 or 5q-   + -7 or 7q-   + +8   + 20q- | * **< 20% blasts** “preleukemia” * usually elderly adults * clonal stem cell dz w. hypercelular marrow but ineffective hematopoiesis (abnormal or dysplastic cells)🡪 resulting in pancytopenia! * **Blood**   + **Pseudo Perger-Huet neutrophils** (2 nuclear lobes)—hyposegmented neutrophil     -not always pathologic   * + MCV frequently >100   + +/- monocytosis (>1000) * Bone Marrow   + Dysplastic cells maybe ↑ blasts   + Ringed sideroblasts—Fe in mitochondria around nucleus (seen w/ Prussian blue stain)     - Always pathologic | | | | | | * complex genetic abnormalities = worse prognosis * 1/3 die from unrelated cause * 1/3 die from MDS complications * **1/3 die from progression to AML** (don't forget to look for t(15;17) if it progresses to AML * 1-3 yr prognosis; T-cell MDS < 1 year | | | | * Two types   + Idiopathic (primary) MDS—no known exposure hx   + Therapy-related (secondary) MDS—2-8 yrs post radiation or chemo | | |
| **Chronic Lymphoproliferative Diseases** | | | | | | | | | | | | | | | | |
| Name | Mutation | | | Diagnosis | | | | Signs/Symptoms | | | | Treatment/Prognosis | | | Other Notes |
| **Chronic Lymphocytic Leukemia (CLL) / Small lymphocytic leukemia (SLL)**  The most common leukemia in adults | * Monoclonal B cells🡪 CD5+ (t-cell ag) , CD10-, CD23+ * Most common genetics if 13q- or trisomy 12 * Bad prognosis –ZAP-70+ or CD38+, 11q- or 17p- | | | * High WBC, absolute lyphocytosis w/ many smudge cells * Nucleus is hypermature—looks like cracked mud * Coombs+ hemolytic anemia = spherocytes * Dx by flow cytometry   + *CD5+, CD10-, CD23+* * Smudge cellsS01871-014-f007 | | | | * **Nonspecific or asymptomatic** * Generalized lymphadenopathy frequent * more common in older aged adults 40-60 y/o | | | | * Bad prognosis –ZAP-70+ or CD38+, 11q- or 17p- * Transform to prolymphocytic leukemia (in blood) or **large cell lymphoma** (Richter syndrome in lymph node—more aggressive) | | |  |
| **Hairy Cell Leukemia (HCL)** | * Dx by flow cytometry (not all HCL look “hairy”)   + +CDLLc,22, 25, 103 | | | * Uncommon, B-cell * Stain w/ TRAP—these are TRAP+ cells * Fuzzy cytoplasm | | | | * **Triad: Older male, massive splenomegaly, pancytopenia** * Bone marrow “dry tap” * TRAP+ cells * more common in older aged adults 40-60 y/o | | | | * Good prognosis * Macintosh HD:Users:elisafuray:Desktop:Screen Shot 2012-12-20 at 9.11.02 AM.png | | |  |

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| **Chronic Myeloproliferative Diseases** | | | | | | |
| Name | Mutation | Diagnosis | Signs/Symptoms | Treatment/Prognosis | Other Notes |
| **Chronic Myelocytic Leukemia (CML)** | * **t(9;22)** Philly chromosome in 100% of cases   + produces a 210 TK | * CBC   + Neutrophilia w/ immature cells   + Basophils ↑   + nRBCs   + WBC > 50,000   + LAP low (High in leukemoid rxn) * **Hypercellular marrow** * Can be very high platelets * Can transform to acute leukemia (blast crisis)   + 2/3 transform to AML   + 1/3 transform to ALL * more common in middle aged adults 40-60 y/o | * Slow onset * Anemia * Hypermetabolism * Weakness * Wt. loss * “dragging”sensation in LUQ from **massive splenomegaly** (have extramedullary hematopoiesis) * pain from infarction | * imatinib (Gleevec) targets the abnormal TK   Accelerated Phase   * dz is transforming into acute leukemia * see worsening anemia and thrombocytopenia * basophils >20% in peripheral blood * blasts >15% in peripheral blood * genetic clonal evolution (do genetic work up)   + 2/3 transform to AML   + 1/3 transform to ALL | * Most common chronic MPD * Adults 50-60 peak   **Leukemoid Reaction** (from bacterial infection  --compare it to CML   * WBC <50,000 * ↑ bands * No basophils * No nRBC * No massive splenomegaly * High LAP (b/c fighting infection and this is assoc. w/ PMN’s) * No t(9:22)   Not very high platelets |
| **Polycythemia vera** | * Jak2 mutation in >95%   + Confirm w/ genetics | * **↑ RBC mass** b/c RBC are growing out of control on their own they don’t need EPO * **high Hb & Hct** * **Low or undetectable EPO** * Normal O2 satuation   + Need to rule out CO poisoning (even though EPO would be ↑ in CO poisoning) | * Red face * Splenomegaly * ↑ blood viscosity and sluding * bleeding and thrombosis w/ infarctions (DVT, strokes, MI, Budd-Chiari Syndrome) | * Transforms to myellofibrosis frequently (burn-out marrow) w/ massive splenomegaly | Types   * **Reactive/relative** (↓ in plasma volume)—associated w/ dehydration) * **Absolute/primary polycythemia rubra vera** (↑ red cell mass; ↓ EPO) * Secondary (↑ EPO)—amt of O2 in ↓ so kidney signal to ↑ EPO—seen in lung dz/smokers or CO poisoning |
| **Primary/Essential Thrombocytosis** | * **Jak2 in 50%**   + **To differentiate from polycythemia vera look at CBC** * **MPL in 10%** (Myeloproliferative leukemia gene) 🡪 works with thrombopoitin gene | * **↑ in platelets** (>600,000 but usually 1 million) * **will see giant platelets** * Dx of exclusion   + Fe def sometimes get platelets >1 million so Fe def is #1 dz to r/o   + CML w/ misleading low WBV but very high platelets | * **Bleeding & thromboses** * Erythromelalgia (red, throbbing burning in hands & feet) * Splenomegaly |  |  |
| **Primary Myelofibrosis** | * **JAK2 mutation in 50%** * **MPL in 5%** | * **Obliterative marrow fibrosis due to megakaryocytes cytokines** * Resulting extramedullary hematopoiesis**🡪 Massive splenomegaly and leukoerythroblastic blood picture**   + Immature myeloid cells in blood (blasts)   + nRBCs in blood | * + Teardrop RBC   Macintosh HD:Users:elisafuray:Desktop:Screen Shot 2012-12-20 at 9.10.42 AM.png |  |  |

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| **Plasma Cell Neoplasms** | | | | | | |
| Name | Pathology | Diagnosis | | Signs/Symptoms | Treatment/Prognosis | Other Notes |
| **Multiple Myeloma/ Plasma Cell Myeloma**   * more common in older aged adults 40-60 y/oMacintosh HD:Users:elisafuray:Desktop:Screen Shot 2012-12-20 at 9.11.52 AM.png | * Plasma cell tumor primarily in the bone and BM * **Plasma cells in BM at least 10% or its MGUS** * IL-6 driven proliferation 🡪 Bone resorption * Tumor cells produce MIP1a (macrophage inflamm protein) which ↑-reg RANKL which activates osteoclasts (leads to 🡪 lytic bone lesions, hypercalcemia, pathologic fractures) * IgG> IgA | * Can get primary amyloidosis if chains depositing in organs * Blood rouleaux   + stack of coins appearance due to ↑ Ig’s in peripheral blood * Serum/urine protein electrophoresis screen for monoclonal protein   + HIV patients will have polyclonal w/ IgG * Immunofixation to type the monoclonal protein (diff MM from WM) * Bone marrow exam * Skeletal survery for lytic lesions * Serum **free** kappa/lambda light chains   + Normal ration 2:1 kappa:lambda if this is out of wack may suggest myeloma | | * Frequent infections (lack of normal Ig’s)---#1 cause of death * Renal Failure #2 cause of death * Bone pain, pathological fractures * lytic bone lesions in axial skeleton * hypercalcemia * pathologic fractures * Hypercalcemia * Myeloma kidney, renal failure (Ig’s clog up tubules) * Need >10% Plasma cells in marrow or is MGUS (uncertain signif) * Hypercalcemia * Bence-Jones proteinuria   + Light chains from plasma cell myeloma that get excreted into urine * Poor prognosis | | * Solitary myeloma (plasmacytoma): bone plasmacytomas progress to multiple myeloma in 10-20 yrs; soft tissue plasmacytoma may be cured by resection * MGUS (monoclonal gammopathy of uncertain significance): BM plasma cell <10%--no lytic lesions, no symptoms; common in patients over 60; may progress to myeloma * Smoldering Myeloma: same as MGUS (asx) w/ 10-30% plasma cells –enough PC’s to be MM but asx |
| **Waldenstrom’s Macroglobulinemia** | * Sx of hyperviscosity due to IgM (IgM builds up in blood and blood gets sludgy)   + Most common in lymphoplasmacytic lymphomas * Plasma cells, lymphocytes and plymphocytes in BM * No bone lesions, no hypercalcemia, * no myeloma kidney or renal failure b/c IgM is too big to be filtered from basement membrane of the glomerulus   Lymphadenopathy, Reynaud’s phenomenon, Hyperviscosity | | | | | |
| **Heavy Chain Dz** |  | | * Usually a small bowel lymphoma |  |  |  |
| **Primary Amyloidosis** |  | | * Free light chains deposited in tissues (organomegaly, large tongue) |  |  |  |
| **Spleen problems** | * Asplasia associated w/ cardiac abnormalities (situs inversus) * Accessory spleens * Autosplenectomy in SS dz b/c the Sickle cells clog up spleen and make in nonfunctional * NO SPLEEN   + Howell-Jolly bodies   + Target cells * Massive Spleen   + CML, HCL, Myelofibrosis, | | | * Rupture common in trauma less commonly w/ infectious mono and malaria * Primary tumors are mostly angiomas (BV tumors) * Acute splenitis—painful w/ blood-borne infections * Infarcts—painful, emboli or SS, wedge shaped * Congestive splenomegaly—mostly w/ cirrhosis or R heart failure   + BF from spleen to liver gets backed up b/c of cirrhosis so spleen enlarges * Hypersplenism may lead to cytopenias by sequestration (Dx: splenomegaly, cytopenia (↓ WBC, or RBC, or platelets), cytopenia corrected by splenectomy) | | |
| **Thymus Problems** | * Thymmic follicular hyperplasia common in myasthenia gravis and other autoimmune dz’s   Tumors:   * thymoma   + Tumor of epithelial cells **(cytokeratin+)**   + Benign, locally invasive and malignant types | | | * + Sx associated w/ pressure on adjacent organs   + Associated w/ myasthenia gravis   + Paraneaplastic sx can include pure red cell asplasia * Germ cell tumors * Lymphoblastic lymphoma (precursor t-cell) | | |

**3 changes to a PMN in acute bacterial infection**

* + Band neutrophil with mild toxic granulation
    - 
  + Dohle body
    - 
  + Vacuolization